

REMARKS

Claims 2-8 and 10 have been canceled, without prejudice. The cancellation of these claims obviates the rejection of these claims. Claim 1 as amended herein is limited to a monoclonal antibody to the amidated peptide of SEQ ID NO:2. Support for this amendment is found throughout the specification, for example at [0025].

Rejection Under 35 U.S.C. § 112

The Examiner has rejected Claims 1, 2, 7-10, 28 and 30 under 35 U.S.C. 112, first paragraph, on the basis that the specification is not fully enabling, commensurate with the scope of the claims. The cancellation of Claims 2, 7 and 8 obviate the rejection of these claims.

The Examiner asserts that, based on the teachings of Couraud et al. (J. Neurochem., 1987, 49:1708-1719), the specification is not enabling for an antibody that specifically binds SEQ ID NO:2. Applicant submits that the specification would enable one of ordinary skill in the art to practice the full breadth of the claimed invention and respectfully traverses the Examiner's rejection.

The Examiner cites Couraud et al. in support of the assertion that "antibodies with the requisite binding specificity are not readily generated" (Office Action, page 5). Couraud et al. disclose a single procedure for preparing the immunogen used to generate antibodies to Substance P (SP). Specifically, Couraud et al. disclose use of bovine serum albumin (BSA) as a carrier and 1, 5-dinitrofluoro-2,4-dinitrobenzene (DFDB) as a coupling agent. The Examiner's attention is respectfully directed to the accompanying Declaration of Ibert C. Wells, the inventor of the present application. It is clear from the Declaration that, as a result of the coupling method reported by Couraud et al., the attachment site of SP to the carrier is via the carboxyl group on

SP and therefore does not allow for the presentation of an amidated carboxyl group to the immune system. Furthermore, it clarifies that Couraud et al. evaluate the cross-reactivity of their five selected monoclonal anti-SP antibodies and polyclonal serum using SP fragments that do not include an amidated carboxyl group (See page 1712).

The present invention claims an isolated monoclonal antibody to SEQ ID NO:2, which is the amidated amino acid sequence Phe-Gly-Leu-Met-NH₂. The instant specification teaches that antigenic substances may vary in their abilities to generate an immune response, and that the host immune system may be boosted by coupling a weak immunogen, such as a peptide, to a carrier. [0029] It further teaches exemplary carriers and means for conjugating a peptide to a carrier [0029]. The Examiner acknowledges that these methods were routine and known in the art (Office Action, page 5). Therefore, Applicant urges that, based on the teachings of the disclosure that the amidated tetrapeptide of SEQ ID NO:2 corrects the magnesium binding defect in erythrocyte membranes ([0022]), one skilled in the art on the filing date of the present application would know how to select a conjugation protocol that links the carrier molecule to the N-terminus of SEQ ID NO:2. Such a methodology would present the amidated C-terminal carboxyl group to the immune system, and thereby enable the skilled artisan to make and use the claimed antibodies.

The Examiner based his rejection regarding antibodies to SEQ ID NO:2 solely on the Couraud et al. reference and the lack of cross-reactivity of Couraud et al.'s polyclonal serum and anti-SP monoclonal antibodies to an amino acid sequence, Phe-Gly-Leu-Met. The Examiner states that Couraud et al. "indicates that antibodies with requisite binding specificity are not readily generated" (Office Action, page 5, emphasis added). However, the fact that some

amount of work must be performed to reach a successful end does not mean that a claimed composition is not enabled.

"Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'

The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. ... The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 8 U.S.P.Q.2d 1400, 1404.

As noted in *Wands*, the need for routine experimentation and screening is allowable and does not mean that an invention is not enabled. Examiner admits that the coupling strategies set forth in the present application involve routine procedures, known in the art. The fact that in order to practice the invention one skilled in the art would need to select from known carrier proteins and conjugating methodologies, and that antibody positive hybridomas would need to be screened for antibodies with the desired reactivity, does not mean that the claimed antibodies are not enabled.

Furthermore, objective enablement, not actual reduction to practice, is all that is required, as stated by the court in *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993):

[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. (emphasis in original) 984 F.2d at 1171-1172.

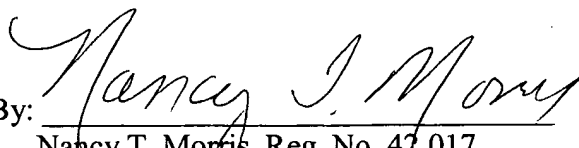
In view of the foregoing, it is urged that the instant specification enables the full breadth of the claims and that no more than routine experimentation is required to practice the claimed invention, and therefore requests that the rejection under 35 U.S.C. 112, first paragraph, be withdrawn.

Rejection Under 35 U.S.C. § 102

The Examiner has rejected Claims 1-6, and 28 and 30 under 35 U.S.C. 102 (b) as being anticipated by Couraud et al. Specifically, that Couraud et al. disclose antibodies that bind polypeptides consisting of SEQ ID NOs:1 and 4. The cancellation of Claims 2-8 obviate the rejection of these claims. The claims herein are limited to an isolated monoclonal antibody that binds (or is cross-reactive with) SEQ ID NO:2. Accordingly, withdrawal of the rejection under Section 102 (b) is respectfully requested.

In view of the foregoing amendments and remarks, it is submitted that the claims remaining for active consideration in this application are free of the cited art and in condition for allowance. Accordingly, favorable action at an early date will be appreciated. If the examiner is of the view that any issue remains unresolved, it is respectfully suggested that applicants undersigned attorney may be contacted by telephone at the number set forth below.

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